Abstract: Calcifying epithelial odontogenic tumor is a benign neoplasm, but its local destructive potential may lead to the formation of major bone defects. Microscopically, there are some histological variants. Among them, we highlight the clear cell variant due to its more aggressive behavior and a higher incidence of relapse. In this context, it is pertinent to describe the clear cell variant of calcifying epithelial odontogenic tumor. Despite the large bone defect formed in the posterior region of the mandible, conservative treatment associated with guided bone regeneration assured complete bone formation and the absence of recurrence in an 8-year follow-up period. (J Oral Sci 56, 95-98, 2014)

Keywords: neoplasm; bone graft; membrane; bone regeneration; retained tooth.

Introduction

Odontogenic calcifying epithelial tumor, also known as Pindborg tumor, was first described as a histopathologically distinct entity in 1955 by the Dutch pathologist Jens Jörgen Pindborg (1). This lesion represents a benign neoplasm of uncertain origin with no etiological factors described, with probable origin in the enamel organ and oral epithelium (2). In addition, it stands out due to its rarity, accounting for only 0.6% to 1.7% of odontogenic tumors (3). However, it raises concerns because of its local aggressive behavior, leading to formation of large bone defects in the jaw (4).

Pindborg tumor is typically located in the posterior region of the mandible and it is most often associated with a retained tooth (1,3). Nevertheless, some peripheral or extraosseous locations have been described (4), accounting for 5% of cases (5), and jaw injuries are occasionally reported. The malignant form of the tumor is extremely rare, with few reports in the literature (2).

The microscopic picture of Pindborg tumor is usually distinctive, composed of epithelial cells and intra- and extracellular calcifications, with an amyloid component in some cases (2). However, an unusual variant characterized by the presence of clear cells has been rarely reported; this variant exhibits more aggressive clinical behavior and generates greater concern regarding the formation of bone defects and relapse (5).

With the advent of implantodontics, there has been much discussion about the use of guided bone regeneration to prevent the development of bone defects and to allow for future rehabilitation with implant-supported prostheses. In this context, many biomaterials are available, such as particulate bovine bone grafts, which are widely used to promote bone regeneration in defects of critical size (6). Disorders affecting the oral and maxillofacial complex may cause the formation of bone defects.
Therefore, it is relevant and important to describe the characteristics of this clinical case of clear cell calcifying epithelial odontogenic tumor, a rare variant with few reports in the literature.

Case Report

The patient, a 51-year-old Caucasian woman with leukoderma, was referred to our clinic complaining of a painless volumetric increase in the left posterior mandibular region first noticed 1 year and 3 months earlier. Clinical examination revealed lesion expansion to the occlusal surface, making it difficult to clean under the pontic of the fixed prosthesis located in the region of tooth 37. Panoramic radiography revealed a unilocular mixed lesion (radiolucent-radiopaque) of considerable size, with scalloped contours involving the retained tooth 37 (Fig. 1). Surgical access was achieved by placing an incision over the crest along with a mesial relief incision, followed by total detachment of the flap. Using high-speed drills under abundant cooled sterile saline, ostectomy was performed, allowing access to the lesion. Total enucleation of the lesion and removal of the retained tooth were performed with the aid of Lucas curettes and the specimen was sent for histopathological examination (Fig. 2). Due to the large size of the bone cavity formed (Fig. 3), particulate bovine bone graft was used (GenOxInorg, Baumer, Brazil) (Fig. 4) combined with a bovine cortical membrane (GenDerm, Baumer, Brazil), in order to promote bone regeneration in the area and prevent development of a significant bone defect. Histopathological examination of the incisional biopsy confirmed the diagnosis of the clear cell variant of calcifying epithelial odontogenic tumor. Microscopically, the lesion was characterized by the presence of islands of eosinophilic epithelial cells in a fibrous stroma and clear cells with hyaline and vacuolated cytoplasm were observed among the calcified nodules (Fig. 5). Polarization microscopy after staining with Congo red confirmed the presence of pink and green amyloid material (Fig. 6). The return following 10 days for suture removal (Fig. 7) Radiographic follow-up of 40 days. (A, B, and C: coronal, axial, and sagittal slices, respectively; the operated area shows appropriate bone density with no recurrence D: 3D reconstruction of the operated area showing complete bone regeneration of bone defect produced after enucleation of the lesion.)

Fig. 1 Initial panoramic radiograph: radiographic appearance of mixed radiopaque-radiolucent lesion comprising the retained tooth 37.

Fig. 2 Specimen sent for histopathological examination.

Fig. 3 Large bone cavity formed after total enucleation of the lesion.

Fig. 4 Filling of bone defect with particulate bovine bone.

Fig. 5 Histological section stained with HE showing areas of clear cells (arrowheads, A) among areas of calcification (arrowheads, B).

Fig. 6 Presence of the pink and green amyloid material confirmed by staining with Congo red.

Fig. 7 Radiograph after 8 years showing no recurrence.

Fig. 8 Radiograph after 8 years showing no recurrence.

Fig. 9 Complete bone regeneration and no recurrence confirmed by computed tomography.

(A, B, and C: coronal, axial, and sagittal slices, respectively; the operated area shows appropriate bone density with no recurrence D: 3D reconstruction of the operated area showing complete bone regeneration of bone defect produced after enucleation of the lesion.)
showed satisfactory healing of the operated area and the radiographic follow-up of 40 days is shown in Fig. 7. The patient was monitored periodically with imaging tests over 8 years and no recurrence was observed (Figs. 8 and 9).

Discussion

Pindborg tumor was classified by the World Health Organization as a benign neoplasm in 1992 (1). This is a rare lesion and its prevalence covers a wide age group, affecting 8- to 92-year-old patients (3). Nevertheless, most of the reported cases comprise patients between the fourth and fifth decades of life (7). The prevalence by race is slightly higher in Caucasians, although there are reports in several populations (5).

Pindborg tumor manifests with asymptomatic slow growth in the maxilla or mandible, leading to late diagnosis and local tissue destruction (2,3). Based on the characteristics described in the literature, the present patient was referred for treatment after complaining of a painless volumetric increase in the left posterior mandibular region. Additionally, according to the patient, the lesion had shown slow growth since it was first noticed 1 year and 3 months previously.

Calcifying epithelial odontogenic tumor is located at the posterior region of the mandible in two thirds of cases, and in most cases (52%) it is associated with a retained tooth (3). Central lesions are more common (95%) and affect mainly the molars, lower premolars (1,4), and mandibular branch (82%) (2). On the other hand, peripheral or extraosseous lesions are rare (5%) and usually affect the gingival portion of the anterior jaws (7). The characteristics observed in this clinical case support the classification of this tumor as a central lesion, where the left posterior mandibular region was affected, more specifically the region of the second molar, which was retained and involved in the lesion.

Due to silent growth and symptomatology, Pindborg tumor is usually discovered incidentally on routine radiographic examination (2). The radiographic features of this lesion include a radiolucent area with dispersed radiopacities throughout its length (4), resembling snowflakes (7). A uni- or multilocular appearance can be observed, similar to a dentigerous cyst or ameloblastoma, respectively (5). Furthermore, in most cases a retained tooth is involved in the lesion (4). These characteristics were observed in the reported case. The radiographic image revealed a mixed radiolucent-radiopaque unilocular appearance, with scalloped contours, around the retained tooth 37.

Microscopically, intraosseous forms can be observed by the presence of epithelial cells with varying amounts of intra- and extracellular calcifications (2). Furthermore, cellular pleomorphism is common (3). More rarely, a clear cell variant of Pindborg tumor has been reported, which usually exhibits more aggressive behavior (4). In the present case, the lesion was characterized by the presence of islands of eosinophilic epithelial cells in a fibrous stroma and clear cells with hyaline and vacuolated cytoplasm were also observed among the calcified nodules. The presence of pink and green amyloid material was confirmed by positivity observed by staining with Congo red. The histological description led to the final diagnosis of the clear cell variant of Pindborg tumor.

Calcifying epithelial odontogenic tumor is considered by many authors to be a benign lesion, but with potential for recurrence and invasion, especially when incompletely removed. Despite its local destructive characteristics, however, it is less aggressive than ameloblastoma, because it does not invade the bone marrow spaces. Nevertheless, the clear cell variant of calcifying epithelial odontogenic tumor exhibits noticeably more aggressive behavior and has higher rates of recurrence (4).

Several variants of calcifying epithelial odontogenic tumor have been described and appear to have different prognoses and therefore require specific treatment (5). Among them, calcifying epithelial odontogenic tumor with Langerhans cells and without calcification, calcifying epithelial odontogenic tumor with cementum- and bone-like mineralization, and clear cell calcifying epithelial odontogenic tumor require special mention (4). The first type resembles the peripheral type, but without calcification and exhibits less aggressive behavior than the extraosseous form. Pindborg tumor with a large amount of calcification is well differentiated and has a more favorable biological behavior. The clear cell variant is the most aggressive type, due to its greater local destructive potential and higher recurrence rate (around 22% of cases). Therefore, some authors no longer consider it to be a benign neoplasm, but rather a low-grade odontogenic carcinoma (5).

Treatment for Pindborg tumor is surgical, and varies from conservative to radical resection (3). According to Nascimento et al. (3), bone margins, even healthy ones, should be included to reduce the chances of relapse. In the present clinical case, conservative surgical removal with total enucleation of the lesion was proposed and appeared to be sufficient, since the lesion had no characteristics of malignancy as some variants of calcifying epithelial odontogenic tumor (4). However, the concerned lesion was considerably large, with expansion to the occlusal and vestibular surfaces observed clinically and radio-
When bone tissue suffers damage, it has the ability to regenerate by itself to a certain extent. However, bone lesions of critical size lead to the formation of fibrous tissue instead of bone, characterizing the development of a bone defect. The defects created during surgical treatment of tumors are examples of this condition (8). In this context, guided bone regeneration is an alternative therapy for the recovery of lost bone tissue by using barriers that correspond to membranes. This prevents the spread of soft tissue among the particles of the material working as a physical barrier, thereby preventing the formation of defects in the area to be healed by new bone formation (9).

The autograft is still considered the gold standard in reconstructive surgery. However, it has some disadvantages, such as limited availability and increased morbidity for the patient (8). In this context, xenografts stand out due to their osteoconductive characteristics as a substitute material in cases where it is not possible and/or convenient to use an autograft. In addition, bone formation achieved through the use of this material seems to be improved when associated with collagen membranes for guided bone regeneration (9). In this clinical case, given the large dimensions of the bone defect formed, it was decided to perform guided bone regeneration combining particulate bovine bone and bovine cortical membrane. The use of a barrier in these situations of large bone defects is of vital importance to avoid development of a residual defect. In this context, the collagen membranes exhibit optimum performance, especially the bovine cortical membrane, which is clinically effective and affordable. This barrier consists of demineralized bovine cortical bone, type I collagen, and growth factors. This material has high biocompatibility and resorbs within 30 days, thus eliminating the need for another surgical approach for its removal (10).

Except for a few reports on calcifying epithelial odontogenic tumors with malignant behavior (4), in most cases the biological behavior is benign and the prognosis is favorable (3) with few cases of relapse (reported in 10 to 15% of subjects) (2,7). Therefore, a follow-up period of at least 5 years is recommended (3). In addition, when it comes to the clear cell variant, greater care should be taken with treatment and follow-up (5). Indolent biological behavior and the absence of relapse were observed in the lesion diagnosed in this study during an 8-year follow-up period, despite being a clear cell variant. However, due to the possibility of late relapse and because of the more aggressive behavior of this variant of Pindborg tumor (8), the patient will continue to be followed up periodically.

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